FDA
TALK PAPER

Food and Drug Administration
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WYETH-AYERST LABORATORIES ANNOUNCES THE WITHDRAWAL OF DURACT FROM THE MARKET

Wyeth-Ayerst Laboratories of St. Davids, Pa. has announced that it is voluntarily withdrawing the analgesic, Duract (bromfenac) from the market. The action follows postmarketing reports of rare severe liver failure in patients in whom the drug was used for extended periods of time which was not in accordance with labeling instructions. The following may be used to respond to questions.

Duract, a non-steroidal anti-inflammatory drug (NSAID), was submitted to the Agency in 1994 and was approved in July 1997 for short term management of acute pain (use for 10 days or less). It was never approved as a treatment for longer term use for chronic conditions such as osteoarthritis or rheumatoid arthritis.

No cases of serious liver injury were reported in clinical trials, however, because there was a higher incidence of liver enzyme elevations in patients treated long term in clinical trials, the product was approved for use for 10 days or less. The information about the elevated liver enzymes was included in the product labeling.

After Duract was marketed, FDA and the company received reports of several cases of rare severe hepatitis and liver failure (some requiring transplantation) in patients taking the drug for more than 10 days.

In February 1998, in response to the reports of severe liver failure (and transplants), FDA and the company strengthened the warnings in Duract's labeling with a special black box warning and Wyeth-Ayerst issued a Dear Doctor letter. The revised label re-emphasized that patients should not take the drug for more than 10 days and alerted physicians and other health care professionals to the cases of severe hepatitis and liver failure (and cases in which patients required a transplant) in patients who had taken Duract.

Despite these efforts, the agency and the company continued to receive reports of severe injuries and death with long term use of Duract.

Given the availability of other therapies, FDA and Wyeth-Ayerst concluded that it would not be practical to implement the restrictions necessary to assure the safe use (less than 10 days) of Duract. The company and FDA agreed that it would be prudent to withdraw the drug from the market. Wyeth-Ayerst is advising doctors to discontinue prescribing and dispensing Duract immediately.

FDA is also advising patients to contact their doctors with any questions about use of the drug. Wyeth-Ayerst is providing the new information in a Dear Doctor letter to physicians, pharmacists,

and health care professionals. Questions from patients or health care professionals about the withdrawal of Duract can be addressed to Wyeth-Ayerst's hotline at 1-800-281-9260.

For more information about the withdrawal of Duract from the market, see:

- "Dear Healthcare Professional" letter
- Wyeth-Averst press release
- "Questions and Answers for Withdrawal of Duract.

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This is the retyped text of a Press Release from Wyeth-Ayerst Laboratories.

FOR IMMEDIATE RELEASE

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DURACT VOLUNTARILY WITHDRAWN

Postmarketing reports of rare, but serious liver events associated with long-term use

ST. DAVIDS, PA -- JUNE 22, 1998 -- Wyeth-Ayerst Laboratories, a division of American Home Products Corporation (NYSE:AHP), today announced the voluntary market withdrawal of DURACT (bromfenac sodium capsules), a nonsteroidal anti-inflammatory analgesic indicated for the short-term (10 days or less) management of acute pain.

The company is taking this action based on postmarketing reports of severe hepatic failure resulting in four deaths and eight liver transplants. All but one of those 12 cases involved patients using DURACT for longer than 10 days -- the maxium recommended duration of treatment. The exception involved a patient with pre-existing significant liver disease.

"We believe this voluntary action is in the best interest of patients," says Dr. Philip de Vane, Vice President, Clinical Affairs and North American Medical Director, Wyeth-Ayerst Laboratories. "While we continue to believe that DURACT is safe and effective when used for 10 days or less, rare but serious adverse events have been associated with DURACT when used for longer periods."

DURACT was introduced in July 1997, and approximately 2.5 million prescriptions have been dispensed -- the great majority of these for 10 days or less. In February 1998, the company and the Food and Drug Administration agreed on labeling changes to further emphasize that DURACT should be used for 10 days or less. These changes were initiated in response to earlier reports of serious events associated with longer-term use.

"Although the revised labeling reduced the number of prescriptions of longer duration and the reports of severe liver events, it did not eliminate them," says Dr. de Vane. "The company has now concluded that further steps to limit use of a potent NSAID pain reliever such as DURACT to just 10 days would not be feasible or effective. In light of these circumstances, as well as the availability of other therapies, Wyeth-Ayerst has decided to withdraw the product."

Wyeth-Ayerst has sent letters of notification to more than 600,000 health care professionals in the United States. They are being advised to stop prescribing and dispensing DURACT immediately. In addition, they have been asked to consider contacting patients who may be using the product longer than 10 days or who have a history of liver disease, and advise these patients to discontinue treatment. Patients are advised to discuss concerns related to DURACT with their physician.

A special information line, 1-800-281-9260, is available to provide answers to questions about DURACT.

Wyeth-Ayers Laboratories, a division of American Home Products Corporation, is a major research-oriented pharmaceutical company.

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This is the retyped text of a letter from Wyeth-Ayerst Laboratories.

June 22, 1998

Dear Healthcare Professional:

Wyeth-Ayerst Laboratories announced today the voluntary market withdrawal of DURACT (bromfenac sodium capsules), a nonsteroidal anti-inflammatory analgesic indicated for the short-term (10 days or less) management of acute pain. The company is taking this action based on postmarketing reports of severe hepatic failure, resulting in four deaths and eight liver transplants.

Approximately 2.5 million prescriptions have been dispensed since DURACT was launched in July 1997. The great majority of those prescriptions were for 10 days or less, a duration of treatment which we continue to believe is safe and effective. All but one of the 12 reported deaths and transplants occurred among the relatively small percentage of patients who took DURACT for more than 10 days. The exception was a person who had pre-existing significant liver disease.

In February 1998, Wyeth-Ayerst Laboratories and the Food and Drug Administration agreed on labeling changes to further emphasize that DURACT should be used for 10 days or less. These changes were initiated in response to earlier reports of serious hepatic events associated with longer-term use. After this action, the number of prescriptions for longer duration use, as well as the number of reported serious hepatic events, was reduced but not completely eliminated. The company has now concluded that further steps to limit use of a potent NSAID analgesic such as DURACT to just 10 days would not be feasible or effective. In light of these circumstances, as well as the availability of other therapies, Wyeth-Ayerst has decided to withdraw this product.

Please discontinue prescribing and dispensing DURACT immediately. You should consider contacting patients who may be taking DURACT for longer than 10 days or who have a history of liver disease. Any such patients should discontinue DURACT treatment. You or your patients may call **1-800-281-9260** with any questions regarding DURACT.

Sincerely,

Philip J. de Vane, M.D.
Vice President, Clinical Affairs
and North American Medical Director

(More information attached)

Sample Returns

Return DURACT samples to:

Wyeth-Ayerst Laboratories
Eaglepointe Center
55 North Pottstown Pike
Eagle, PA 19480

For UPS Shipping information, or if you have any other questions, please call Wyeth-Ayerst Laboratories at **1-800-281-9260**.

Pharmacists will receive additional correspondence within the next few days concerning returning product for credit.

Wyeth-Ayerst Laboratories

Division of American Home Products Corporation
PO Box 8299
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